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**DEPARTMENT: ANATOMY**

**MATRIC NO: 16/MHS06/043**

**LEVEL: 400**

**COURSE CODE: ANA 404**

**COURSE TITLE: INTRODUCTION TO HISTOPATHOLOGY**

**COURSE LECTURER: MR. EDEM E. EDEM**

**TOPIC: WRITE A COMPREHENSIVE REVIEW OF THE AETIOLOGY OF COVID-19, ITS PATHOGENESIS, HISTOPATHOLOGICAL FEATURES AND THE CURRENT POTENTIAL THERAPIES TO ADDRESS IT. ALSO COMMENT ON THE FUTURE OF COVID-19 ON PUBLIC HEALTH.**

**DATE: 15th APRIL, 2020.**

**Introduction**

Coronaviruses (CoVs), of the family Coronaviridae, are enveloped viruses with a single-strand, positive-sense RNA genome approximately 26–32 kilobases in size, which is the largest known genome for an RNA virus (Weiss and Navas, 2005). The term ‘coronavirus’ refers to the appearance of CoV virions when observed under electron microscopy, in which spike projections from the virus membrane give the resemblance of a crown, or corona in Latin (Lai and Cavanagh, 1997). Coronaviruses cause respiratory and intestinal infections in animals and humans (Masters and Perlman, 2013), and they were not considered to be highly pathogenic to humans until the outbreak of severe acute respiratory syndrome (SARS) in 2002 and 2003 in Guangdong province, China (Zhong *et al.,* 2003; Drosten *et al.,* 2003; Fouchier *et al.,* 2003; Ksiazek, *et al.,* 2003), as the coronaviruses that circulated before that time in humans mostly caused mild infections in immunocompetent people. Ten years after SARS, another highly pathogenic coronsavirus, Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in Middle Eastern countries (Zaki *et al.,* 2012).

**Etiology**

On the ninth of January 2020, the World Health Organization (WHO) confirmed that SARS-CoV-2 was the cause of COVID-19 (which was formerly referred to as 2019-nCoV) (Wu *et al.,* 2020). It is a member of the Betacoronavirus genus, one of the genera of the Coronaviridae family of viruses. Coronaviruses are enveloped single-stranded RNA viruses that are found in humans, mammals and birds. These viruses are responsible for pulmonary, hepatic, neurological, and intestinal disease.

As with many human infections, SARS-CoV-2 is zoonotic. The closest animal coronavirus by genetic sequence is a bat coronavirus, and this is the likely ultimate origin of the virus (*Chen et al.,* 2020; Wang *et al.,* 2020). The disease can also be transmitted by snakes (Pan *et al.,* 2020). Six coronaviruses are known to cause human disease. Two are zoonoses: the severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), both of which may sometimes be fatal. The remaining four viruses cause the common cold and this includes: HCoV-OC43, and HCoV-HKU1 (betaCoVs of the A lineage); HCoV-229E, and HCoV-NL63 (alphaCoVs).

**Pathogenesis**

The severe symptoms of COVID-19 are associated with an increasing numbers and rate of fatalities specially in the epidemic region of China. On January 22, 2020, the China National Health Commission reported the details of the first seventeen deaths and on January 25, 2020 the death cases increased to fifty-six deaths (Wang et al., 2020). The percentage of death among the reported 2684 cases of COVID-19 was approximately 2.84% as of Jan 25, 2020 and the median age of the deaths was seventy-five (ranging from 48–89) years (Wang *et al.,* 2020).

Patients infected with COVID-19 showed higher leukocyte numbers, abnormal respiratory findings, and increased levels of plasma pro-inflammatory cytokines. One of the COVID-19 case reports showed a patient at five days of fever presented with a cough, coarse breathing sounds of both lungs, and a body temperature of 39.0 °C. The patient's sputum showed positive real-time polymerase chain reaction results that confirmed COVID-19 infection (Lei *et al.,* 2020). The laboratory studies showed leucopenia with leukocyte counts of 2.91 × 10^9 cells/L of which 70.0% were neutrophils. In addition, a value of 16.16 mg/L of blood C-reactive protein was noted which is above the normal range (0–10 mg/L). High erythrocyte sedimentation rate and D-dimer were also observed (Lei et al., 2020). The main pathogenesis of COVID-19 infection as a respiratory system targeting virus was severe pneumonia, RNAaemia, combined with the incidence of ground-glass opacities, and acute cardiac injury (Huang *et al.,* 2020).

Significantly high blood levels of cytokines and chemokines were noted in patients with COVID-19 infection that included IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA. Some of the severe cases that were admitted to the intensive care unit showed high levels of pro-inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα that are reasoned to promote disease severity (Huang et al., 2020).

**Histopathological features of covid-19 and the current** **potential therapies to address it**

A recent article described the early histopathological features in COVID-19 in two patients who underwent surgical resections for lung adenocarcinoma but were later discovered to have had COVID-19 at the time of the operation (Tian *et al.,* 2020). The findings were non-specific and included oedema, pneumocyte hyperplasia, focal inflammation and multinucleated giant cell formation while no hyaline membranes were seen. Given that these patients were asymptomatic with respect to COVID-19 at the time of the operation, these are likely to reflect only early changes of acute lung injury in the infection (Tian et al., 2020). In another case, a 50-year-old man died from severe COVID-19 infection and more marked histopathological findings were noted (Xu *et al.,* 2020). Samples were taken by postmortem biopsy, and a description of the gross postmortem findings were not given, although multiple ground glass opacities were noted. The microscopic findings included diffuse alveolar damage with exudates (Xu *et al*., 2020) while the inflammation was predominantly lymphocytic, and multinucleated giant cells were seen alongside large atypical pneumocytes, although no definitive viral inclusions were noted. Microvesicular steatosis with mild inflammation was also noted in the liver, although it was unclear whether this was related to the virus or iatrogenic. The features are very similar to the features seen in SARS and MERS-coronavirus infections (Ding *et al.,* 2003).

**Potential therapies**

So far there are no specific medications for COVID-19, but some drugs and therapies have been proven to be effective in treating patients. The number of potential therapeutic options for treatment of COVID-19 is growing. Approaches include blocking SARS-CoV-2 from entering cells, disrupting the virus replication, antivirals, vaccines, and suppressing overactive immune response (Haiou *et al.,* 2020).

**1.Favipiravir**

It is an antiviral drug developed in Japan to be used against many viruses built around ribonucleic acid; a substance essential for human life, including the novel coronavirus.

Chinese researchers have completed clinical studies of Favipiravir, which shows promising clinical efficacy in treating novel coronavirus pneumonia, said by Zhang Xinmin, head of the China National Center for Biotechnology Development on March 17. Experiments have shown that patients treated with Favipiravir recovered more quickly and their lung conditions improved better than patients in the control group.

The Third People’s Hospital of Shenzhen in Guangdong province conducted a clinical trial on eighty patients, with thirty-five receiving the drug. The results showed that patients who took Favipiravir tested negative within four days of treatment, whereas patients in the control group needed eleven days to test negative. The lung conditions of 91.4 percent of the treated group improved, compared with 62.2 percent of the control group, Zhang said. In terms of safety, Zhang said it has shown no obvious adverse effects.

**2. Chloroquine phosphate**

Developed in the 1950s to treat malaria, the drug has shown the potential to inhibit coronavirus growth during in vitro tests. China’s leading epidemic control expert, Zhong Nanshan, “said early clinical results show that severe patients have recovered more quickly after taking the medicine compared to other drugs”.

**3. Plasma transfusion therapy**

Convalescent plasma collected from patients who have recovered from COVID-19 contains antibodies that are effective in combating the virus.

Plasma transfusion therapy has been used to treat critically ill patients infected with the novel coronavirus in China. As of March 8, more than one thousand recovered patients have donated more than 350,000 milliliters of plasma to help save other patients and about 200 to 300 milliliters of pure plasma are drawn from donors each time.

As plasma donated from recovered patients is in short supply and involves a complicated processing procedure and high costs, its use is mainly limited to the treatment of severe patients.

**4. Remdesivir**

Remdesivir is an antiviral medication developed by US biotechnology company Gilead Sciences as a treatment for Ebola, although it is not being tested as a potential COVID-19 treatment.

Cao Bin, who leads the trials in China, said studies have shown that “Remdesivir is effective in arresting the growth of the coronavirus in vitro, which means the procedure was conducted in a controlled environment outside of a living organism”.

**5. Traditional Chinese medicine**

Traditional Chinese medicine has also played a big role in the prevention and treatment of COVID-19. More than 90 percent of patients infected with the novel coronavirus in China have been treated with Traditional Chinese Medicine.

**Future of covid-19 on public health**

The epidemic of coronavirus disease 2019 (COVID-19), originating in Wuhan, China, has become a major public health challenge for not only China but also countries around the world. The World Health Organization announced that the outbreaks of the novel coronavirus have constituted a public health emergency of international concern. The public health crisis caused by the rapid spread of COVID-19 is having very profound impacts on societies throughout the world, and will continue to do so for years to come (Erausquin, 2020).

Public health often has hidden functions which happens in the background, and yet they save so many lives. For example, infection control measures in hospitals have completely changed our ability to provide safe and effective medical treatments we now take for granted. Vaccines are a huge benefit and have been incredibly important for child health. Hopefully, these public health measures to slow the spread of COVID-19 will be viewed positively in the future, and that the field of public health will also be viewed positively. It’s also possible that because of the implementation of these infection control measures, including social distancing and the cancelling of events, there will be a pretty flat epidemic curve in some areas of the country (Erausquin, 2020).

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